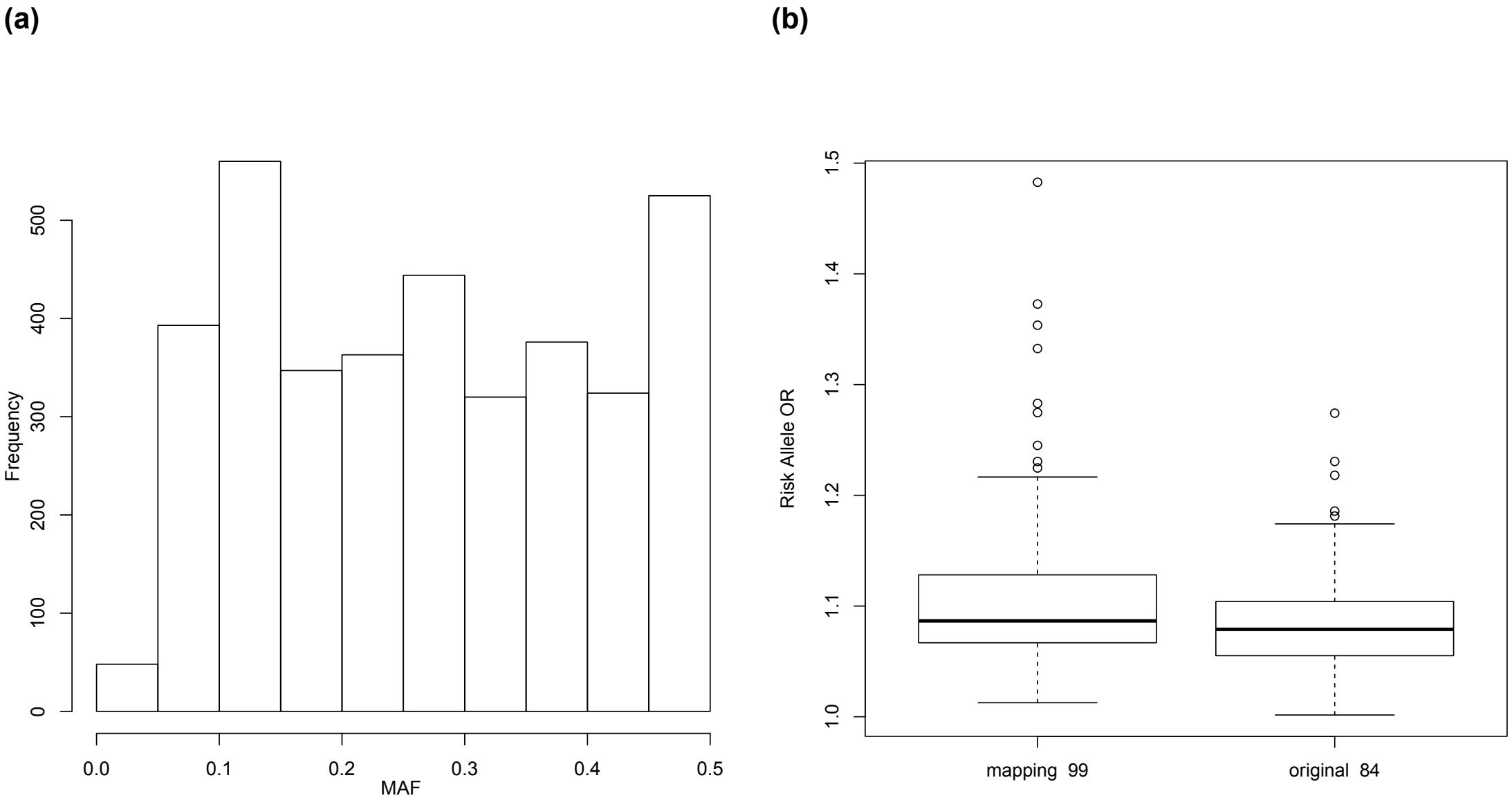
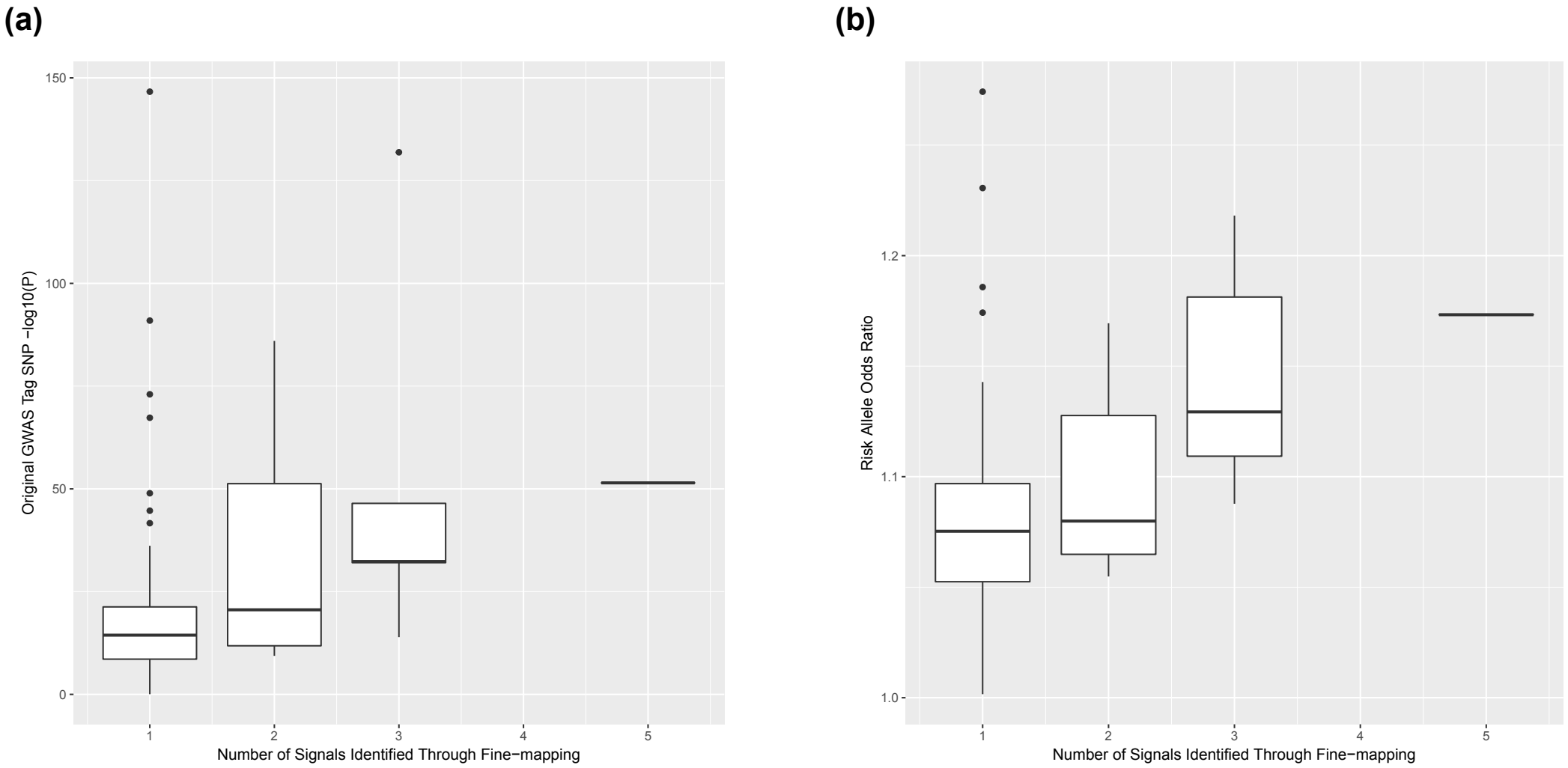
Supplementary Figure 1



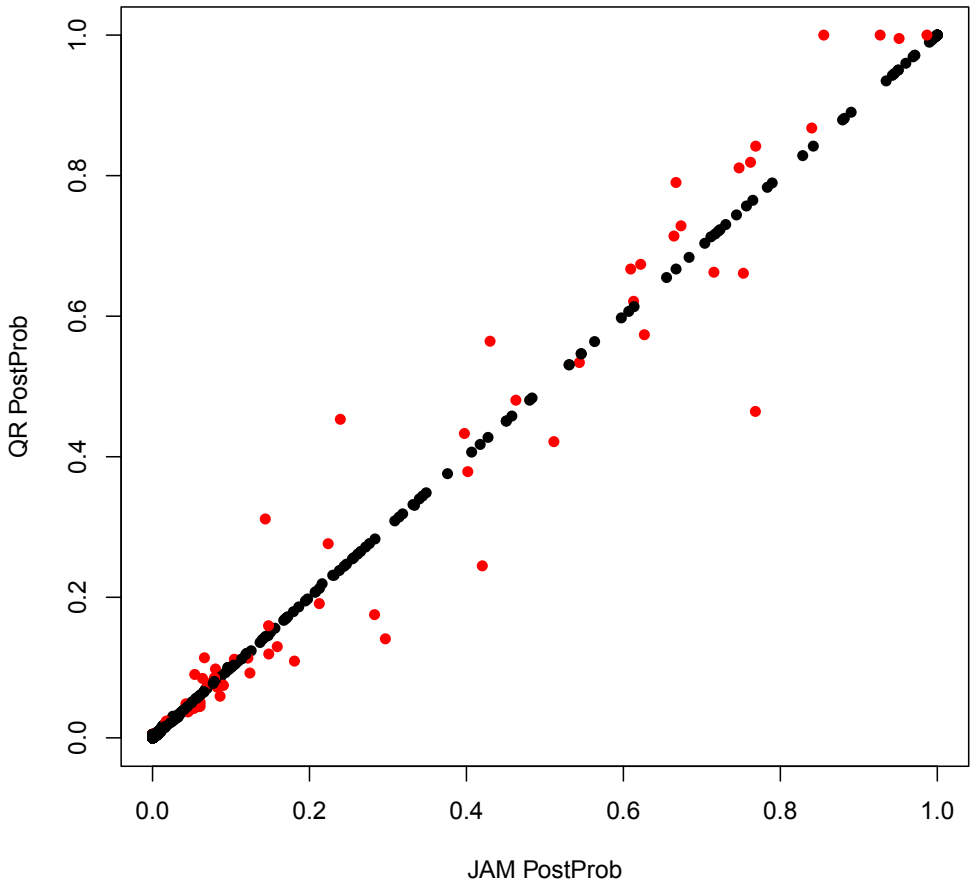
Supplementary Figure 1 – (a) Minor allele frequency distribution of variants within the 95% credible set selected by JAM. **(b)** Odds ratios of the 84 original GWAS tag SNPs replicated in Europeans relative to the 99 novel representative lead SNPs identified through fine-mapping. Single variants representing the 99 independent signals were established using the procedure described for familial relative risk calculation. The high odds ratio variant rs138213197 at *HOXB13* is omitted from this plot for greater clarity at the remaining regions with lower effect sizes. Box plot centre lines represent the median odds ratios for each variant set. Lower and upper hinges represent the first and third quartiles respectively, with whiskers denoting the largest and smallest values within 1.5 IQR (interquartile range) of the quartiles and outlying values plotted as individual points.

Supplementary Figure 2



Supplementary Figure 2 – Comparison of the number of signals identified through subsequent Bayesian fine-mapping with **(a)** *P*-values and **(b)** Odds Ratios in the original meta-analysis for the 84 European replicated original GWAS tag SNPs.
The high odds ratio variant rs138213197 at *HOXB13* is omitted from these plots for greater clarity at the remaining regions with lower effect sizes. Box plot centre lines represent the median *P*-value or odds ratios for regions containing different numbers of independent signals. Lower and upper hinges represent the first and third quartiles respectively, with whiskers denoting the largest and smallest values within 1.5 IQR (interquartile range) of the quartiles and outlying values plotted as individual points.

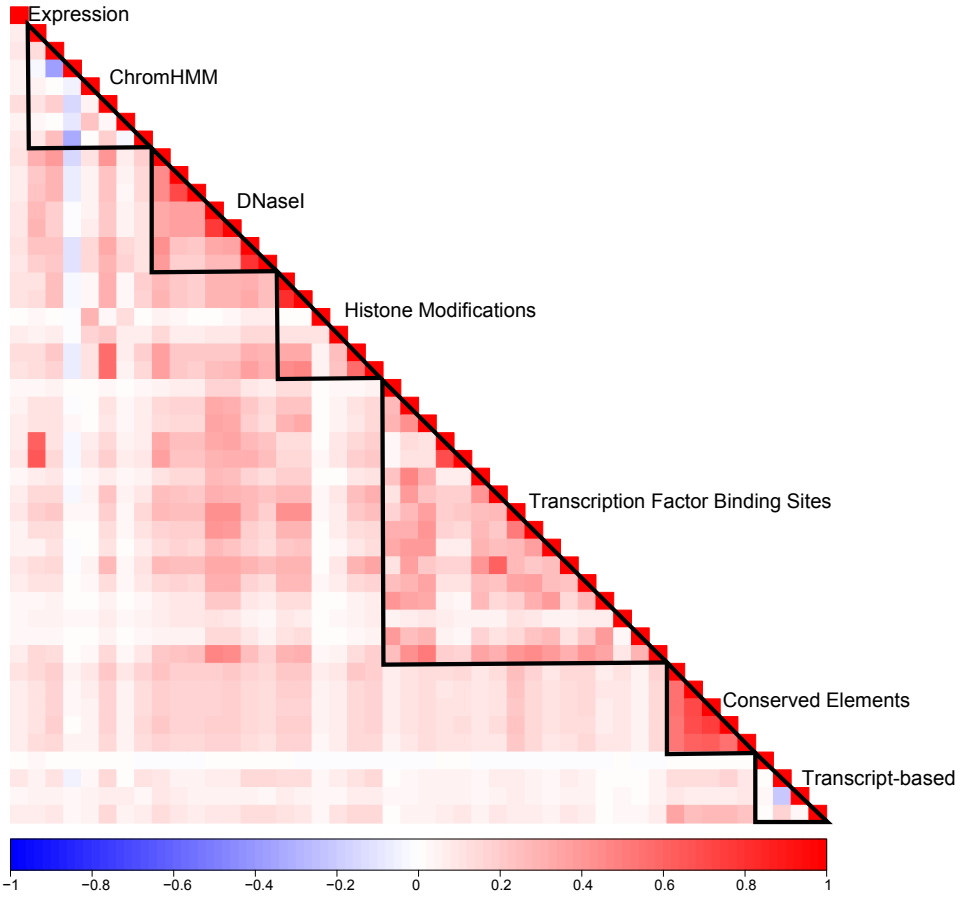
Supplementary Figure 3



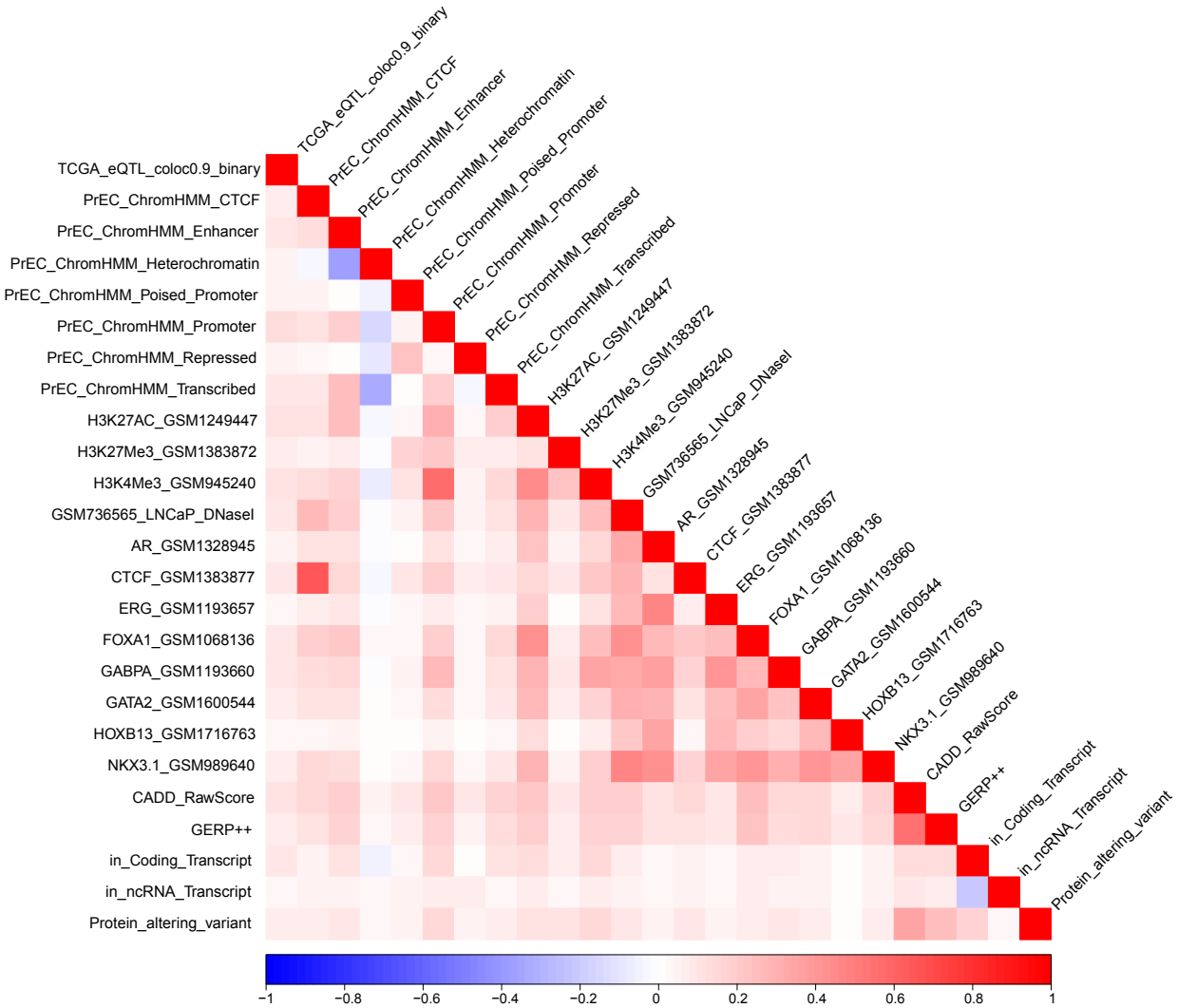
Supplementary Figure 3 – Overview of tag variant posterior probabilities recalculated during Quantile Regression across all 75 regions included in this analysis. Tags marked in red were adjusted by ΔPosterior probability$_{QR}$ ≥ ±0.005 based on annotations associated across the upper quantiles of the posterior probability distribution.

Supplementary Figure 4

(a)



(b)



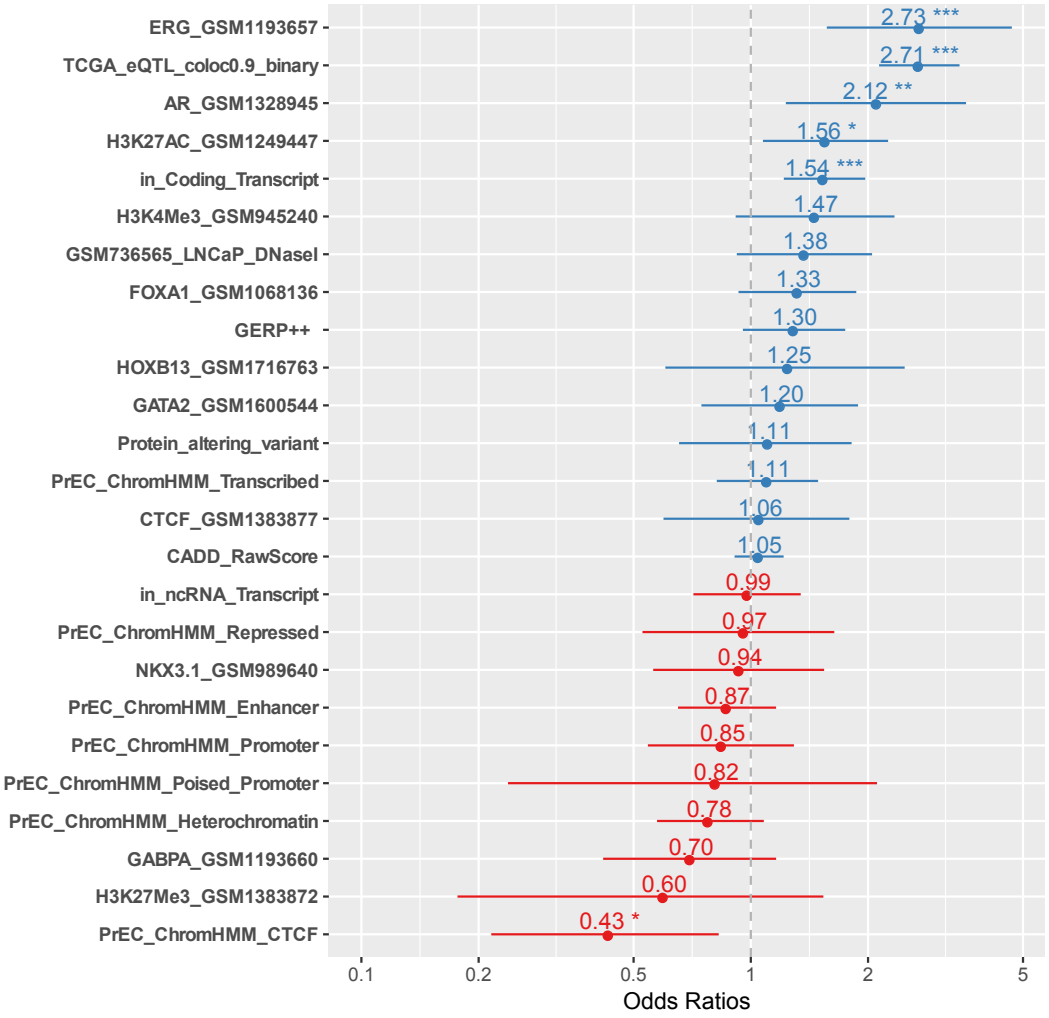
Supplementary Figure 4 – (a) Correlation between annotation categories is shown for priority pruner tags, which inherit annotations for all of their respective proxy variants. **(b)** Correlation between the individual annotations used in the Quantile Regression analysis, for which a single informative dataset was selected for each annotation group to avoid inclusion of datasets representing the same information class.

Supplementary Figure 5

(a)

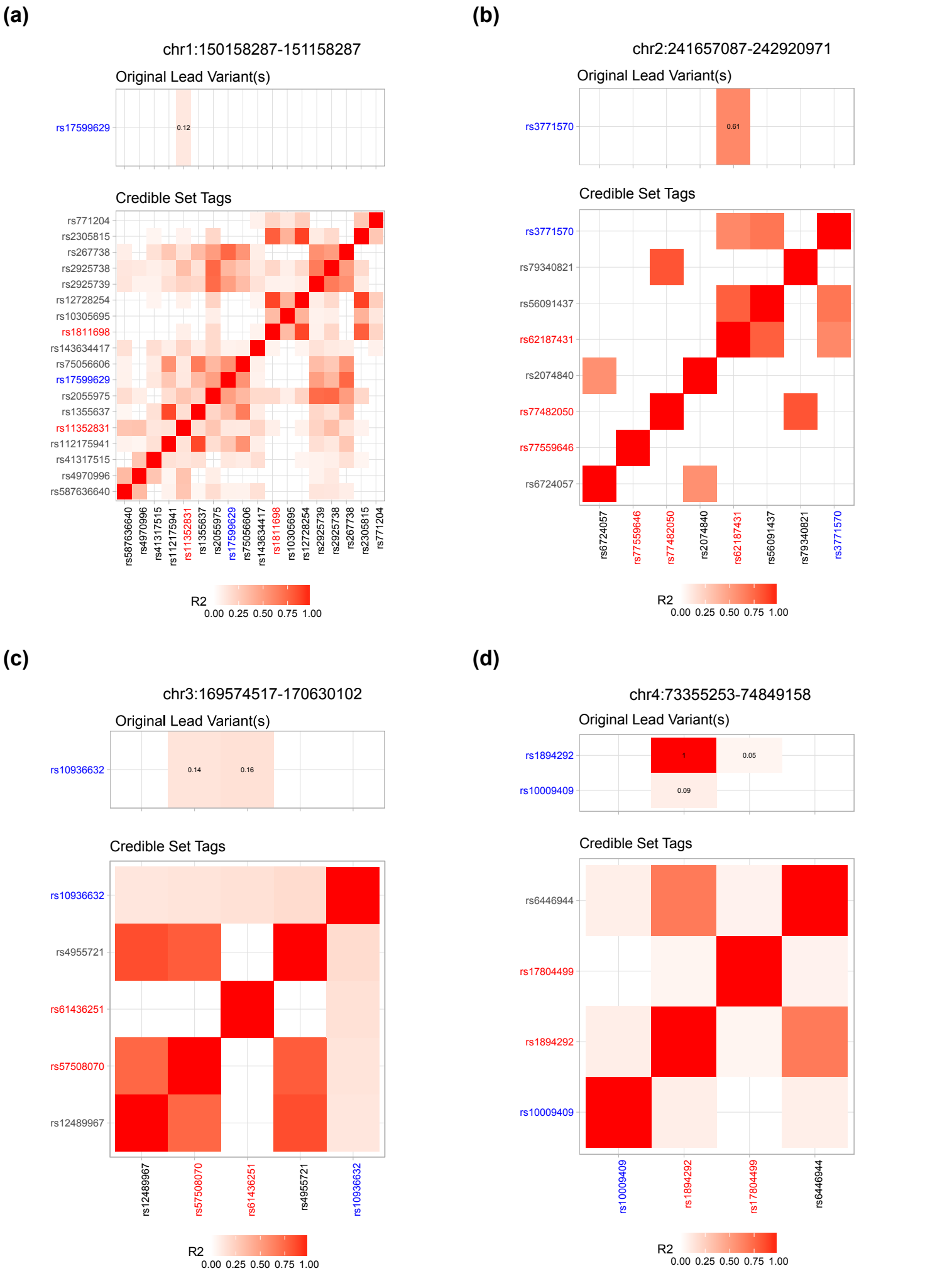
	Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	-5.23448	0.16680	-31.383	< 2e-16	***
PrEC_ChromHMM_CTCF	-0.83398	0.34150	-2.442	0.014603	*
PrEC_ChromHMM_Enhancer	-0.13724	0.14780	-0.929	0.353110	
PrEC_ChromHMM_Heterochromatin	-0.24523	0.16075	-1.526	0.127118	
PrEC_ChromHMM_Poised_Promoter	-0.20273	0.54338	-0.373	0.709086	
PrEC_ChromHMM_Promoter	-0.16644	0.22030	-0.756	0.449920	
PrEC_ChromHMM_Repressed	-0.03525	0.28774	-0.122	0.902507	
PrEC_ChromHMM_Transcribed	0.10251	0.15266	0.672	0.501890	
GSM736565_LNCaP_DNaseI	0.32281	0.20392	1.583	0.113414	
AR_GSM1328945	0.75119	0.27154	2.766	0.005667	**
CTCF_GSM1383877	0.05604	0.27992	0.200	0.841318	
ERG_GSM1193657	1.00400	0.27891	3.600	0.000319	***
FOXA1_GSM1068136	0.28245	0.17760	1.590	0.111752	
GABPA_GSM1193660	-0.35188	0.26055	-1.351	0.176844	
GATA2_GSM1600544	0.18173	0.23585	0.771	0.440981	
HOXB13_GSM1716763	0.22586	0.35916	0.629	0.529438	
NKX3.1_GSM989640	-0.06221	0.25740	-0.242	0.809021	
TCGA_eQTL_coloc0.9_binary	0.99863	0.12126	8.235	< 2e-16	***
CADD_RawScore	0.05195	0.07398	0.702	0.482577	
GERP++	0.25948	0.15431	1.682	0.092662	.
H3K27AC_GSM1249447	0.44695	0.18880	2.367	0.017921	*
H3K27Me3_GSM1383872	-0.51028	0.53817	-0.948	0.343042	
H3K4Me3_GSM945240	0.38463	0.23950	1.606	0.108285	
in_Coding_Transcript	0.43440	0.12286	3.536	0.000407	***
in_ncRNA_Transcript	-0.01336	0.16155	-0.083	0.934115	
Protein_altering_variant	0.10779	0.25930	0.416	0.677645	

(b)



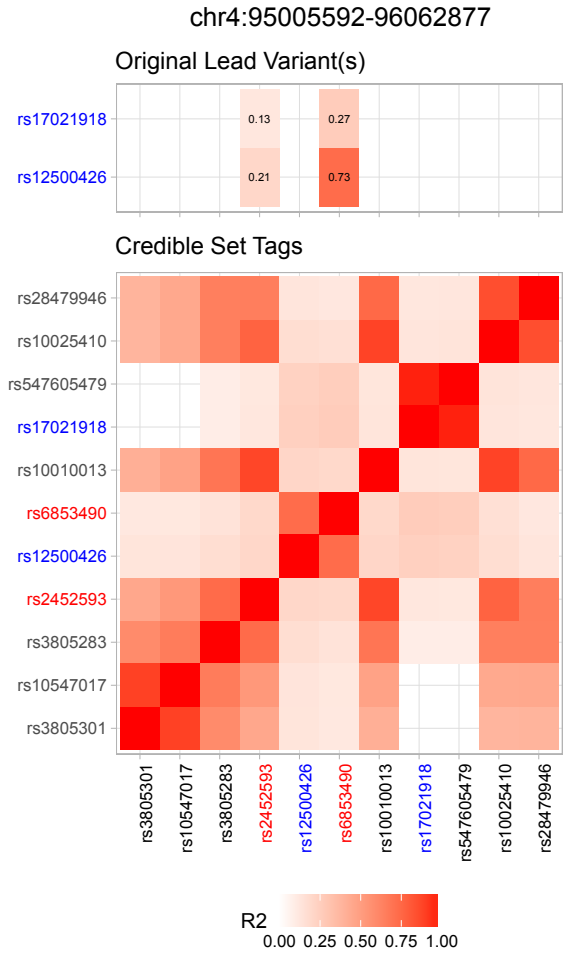
Supplementary Figure 5 – Results of logistic regression across the individual annotations used in the Quantile Regression analysis, for which a single informative dataset was selected for each annotation category to avoid inclusion of datasets representing the same information class. **(a)** Logistic regression model coefficient output. For each annotation feature covariate, variable coefficients ("Estimate") and standard errors ("Std. Error") are shown, alongside their corresponding z-statistic ("z value") and two-tailed *P*-values ("Pr(>|z|)"). **(b)** Dot plot of odds ratio estimates and 95% confidence intervals for each annotation feature in the logistic regression model. For both panels, single, double or triple star symbols denote annotation features nominally significant at $P < 0.05$, 0.01 and 0.001 thresholds respectively.

Supplementary Figure 6

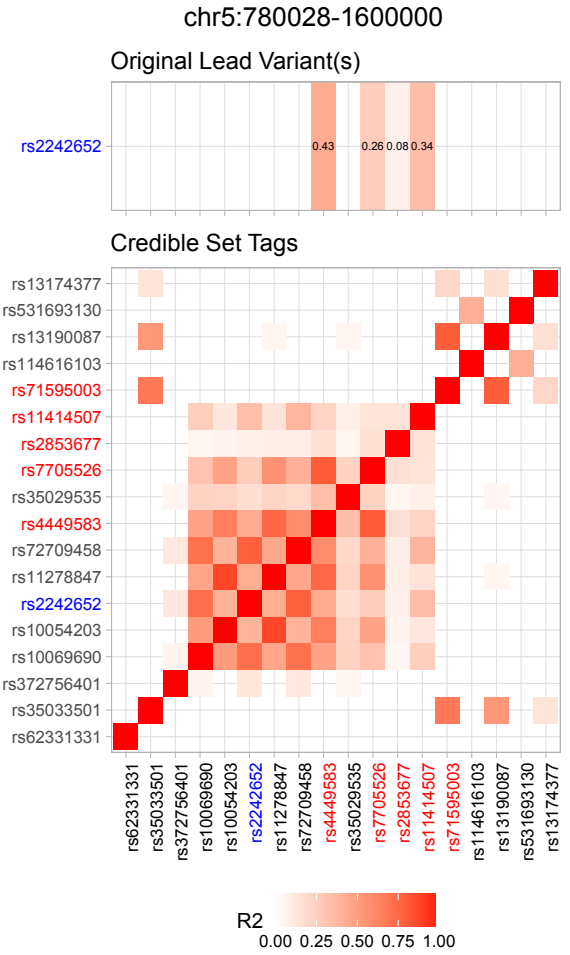


Supplementary Figure 6 (continued)

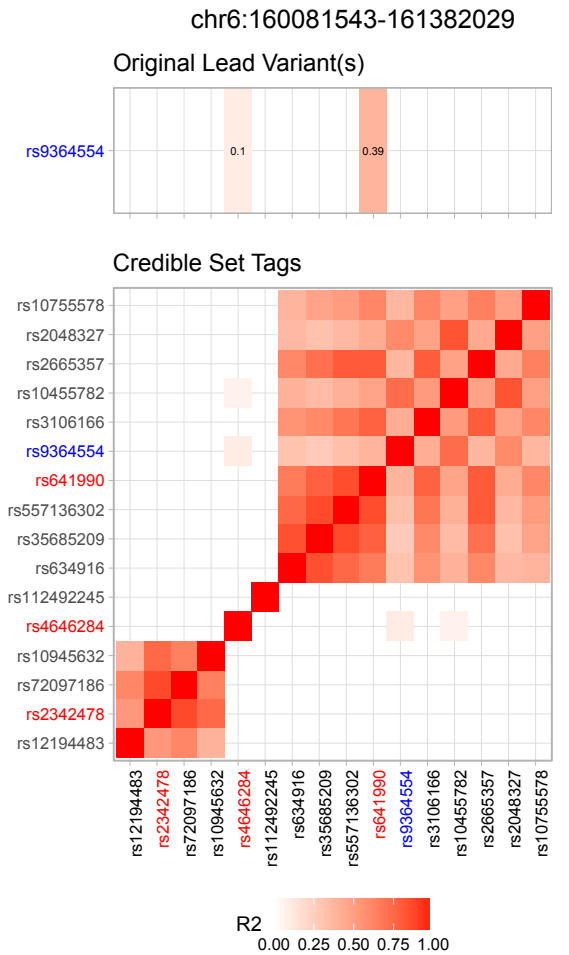
(e)



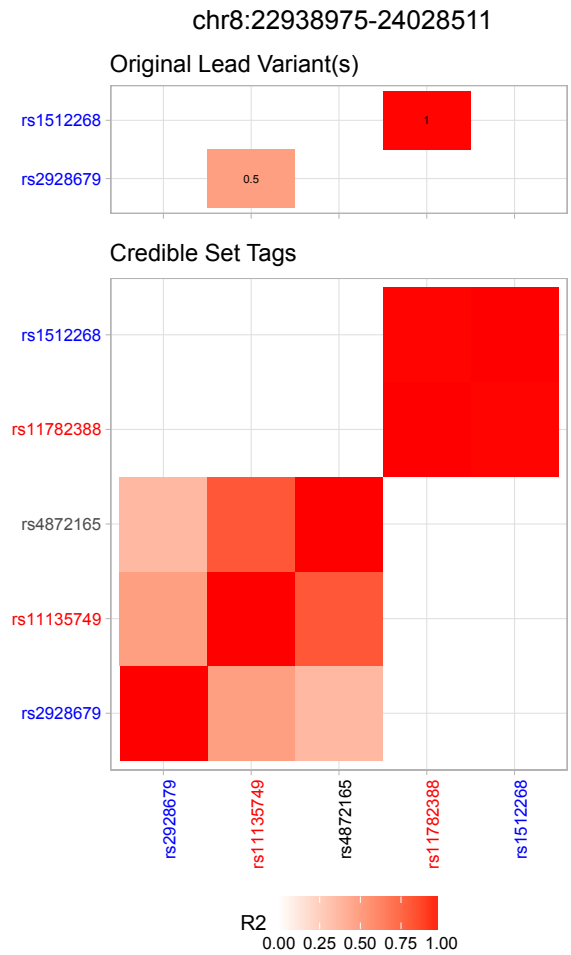
(f)



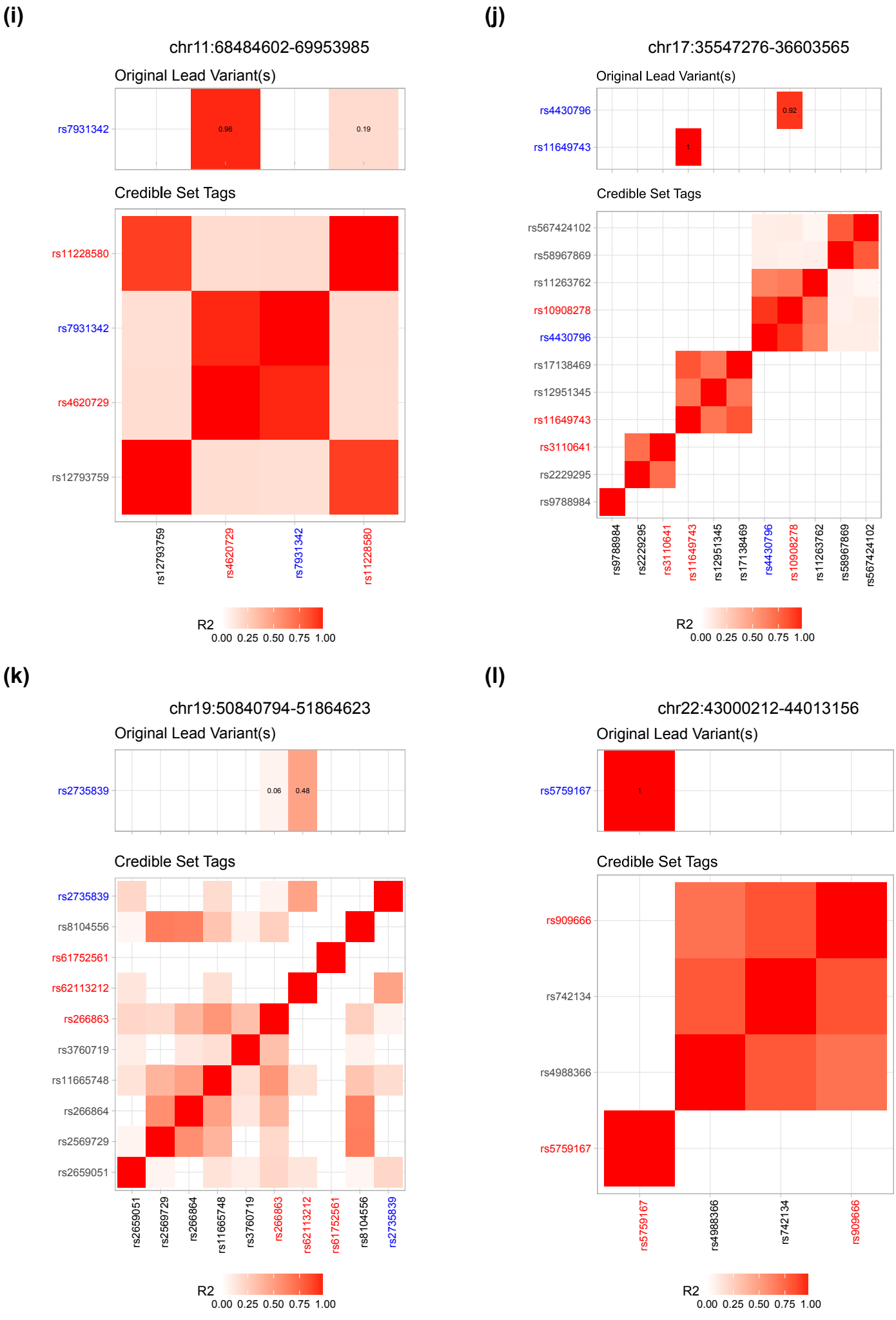
(g)



(h)

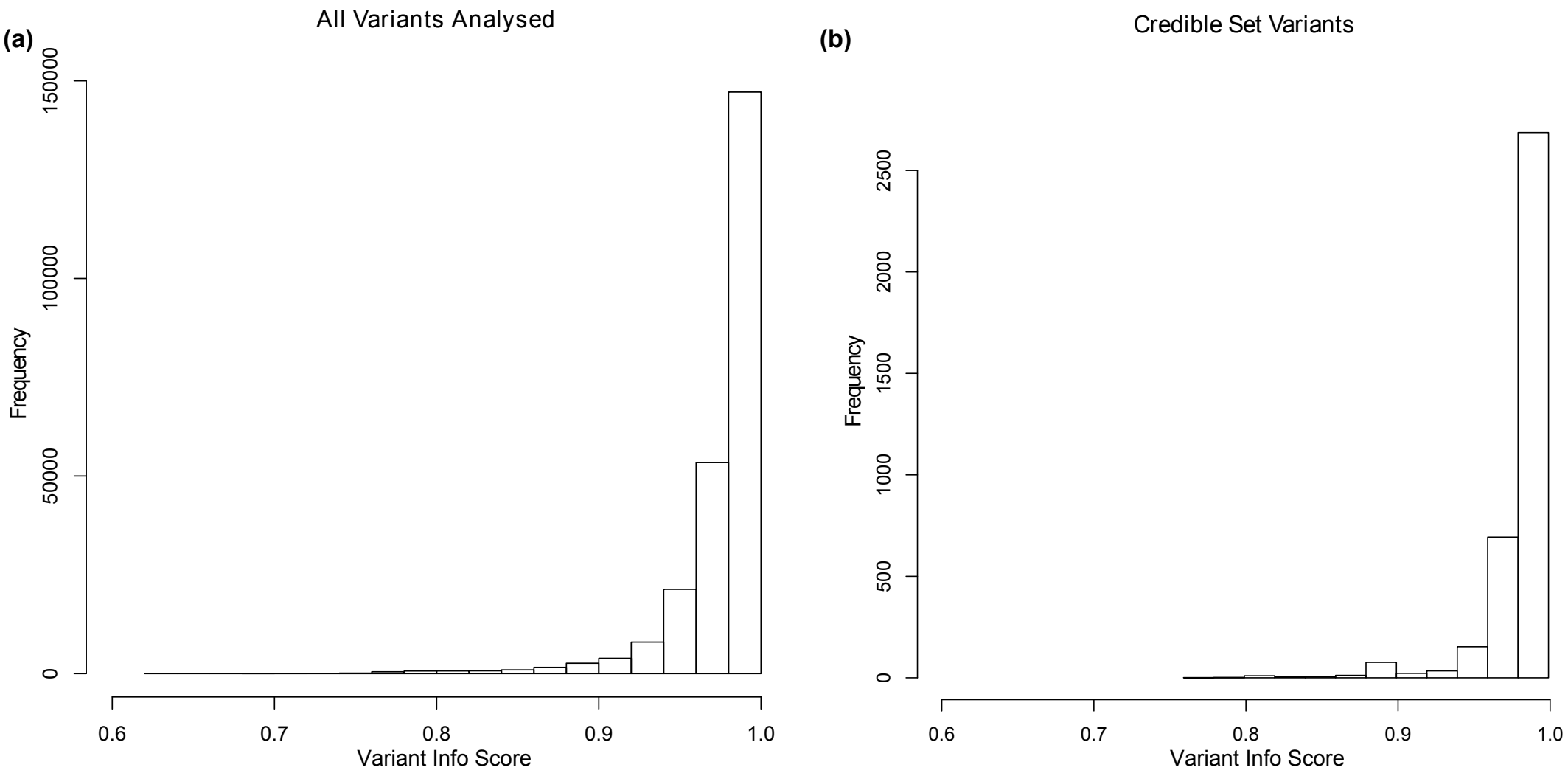


Supplementary Figure 6 (continued)



Supplementary Figure 6 – Heat-map plot depicting LD between the original index SNPs and tag variants included in the credible set for regions containing multiple independent signals. The 12 regions identified to contain multiple independent signals by JAM are depicted in separate panels **(a-l)**. Original index SNPs are denoted in blue and the combination of tags given the greatest posterior support by JAM, which were taken as representative variants for the individual independent signals during the FRR calculation, are shown in red. The Original Lead Variant(s) track shows LD between the original GWAS SNP(s) and FRR representative variants. The Credible Set Tags grid depicts LD between all tag variants selected in the credible set; the original index SNP is also included if it was not selected in the final credible set or was represented by another tag.

Supplementary Figure 7



Supplementary Figure 7 – Histogram of variant Info scores in the imputed meta-analysis data after QC filtering. **(a)** All variants analysed during fine-mapping. **(b)** Variants within the 95% credible set selected by JAM.

Region Boundary	SNPs Mapped	Lowest *P* Value of any SNP in Region in EUR meta-analysis	Comments
chr1:10056097-11056097	rs636291 (*PEX14*)	3.88×10^{-7}	Previously reported for young onset PrCa only
chr9:123927373-125154402	rs1571801 (*DAB2IP*)	3.05×10^{-4}	Previously reported for aggressive PrCa only
chr14:60622526-61622526	rs7153648 (*SIX1*)	7.74×10^{-5}	Previously reported in a multi-ethnic meta-analysis only
chr16:71191329-72191329	rs12051443 (*PHLPP2*)	3.98×10^{-5}	Previously reported in a multi-ethnic meta-analysis only
chr19:54204670-55297848	rs103294 (*LILRA3*)	7.16×10^{-4}	Previously reported in a Chinese population only

Supplementary Table 1 – List of previously published PrCa GWAS associations that were not replicated in our European meta-analysis prior to fine-mapping. The previously reported association was considered replicated if any variant(s) within the assigned fine-mapping region boundary had a marginal *P*-value beyond the threshold specified for genome-wide significance of association with PrCa ($P<5\text{x}10^{-8}$).

	Beta-Binomial(1,P) Prior probability			
Number of Variants in region (P)	**No effect**	**≥1 effect**	**≥2 effects**	**≥3 effects**
5	0.5	0.5	0.22	0.08
10	0.5	0.5	0.24	0.11
100	0.5	0.5	0.25	0.12
1000	0.5	0.5	0.25	0.12

Supplementary Table 2 – Beta-binomial prior probabilities for different numbers of independent causal variants as a function of the number of variants in a region.

Supplementary Note 1 – Funding & Acknowledgements. Information and acknowledgements for consortia contributing to the meta-analysis and for individual study groups within the PRACTICAL Consortium.

GWAS Studies in the Meta-Analysis Dataset

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CPCS1 & CPCS2
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